General

Guideline Title

The role of surgery in the management of patients with diffuse low grade glioma: a systematic review and evidence-based clinical practice guideline.

Bibliographic Source(s)

Aghi MK, Nahed BV, Sloan AE, Ryken TC, Kalkanis SN, Olson JJ. The role of surgery in the management of patients with diffuse low grade glioma: a systematic review and evidence-based clinical practice guideline. J Neurooncol. 2015 Dec;125(3):503-30. [69 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The rating schemes used for the strength of the evidence (Class I-III) and the levels of recommendations (Level I-III) are defined at the end of the "Major Recommendations" field.

Question

Should patients with imaging suggestive of low grade glioma undergo observation versus treatment involving a surgical procedure?

Target Population

These recommendations apply to adults with imaging suggestive of a World Health Organization (WHO) grade II glioma (oligodendroglioma, astrocytoma, or oligo-astrocytoma).

Recommendation

Surgical resection is recommended over observation to improve overall survival for patients with diffuse low grade glioma (*Level III*) although observation has no negative impact on cognitive performance and quality of life (*Level II*).

Question

What is the impact of extent of resection on progression free survival (PFS) or overall survival (OS) in low grade glioma patients?

Target Population

These recommendations apply to adults with imaging suggestive of a WHO grade II glioma (oligodendroglioma, astrocytoma, or oligo-astrocytoma).

Recommendations

Impact of Extent of Resection on PFS

Level II. It is recommended that gross total resection (GTR) or subtotal resection (STR) be accomplished instead of biopsy alone when safe and feasible so as to decrease the frequency of tumor progression recognizing that the rate of progression after GTR is fairly high.

Impact of Extent of Resection on OS

Level III. Greater extent of resection can improve OS in low grade glioma patients.

Question

What tools are available to increase extent of resection in low grade glioma patients?

Target Population

These recommendations apply to adults with imaging suggestive of a WHO grade II glioma (oligodendroglioma, astrocytoma, or oligo-astrocytoma).

Recommendation

Intraoperative Magnetic Resonance Imaging (MRI) during Surgery

Level III. The use of intraoperative MRI should be considered as a method of increasing the extent of resection of low grade gliomas.

Question

What is the impact of surgical resection on seizure control and accuracy of pathology in low grade glioma patients?

Target Population

These recommendations apply to adults with imaging suggestive of a WHO grade II glioma (oligodendroglioma, astrocytoma, or oligo-astrocytoma).

Recommendations

Surgical Resection and Seizure Control

Level III. After taking into account the patient's clinical status and tumor location, gross total resection is recommended for patients with diffuse low grade glioma as a way to achieve more favorable seizure control.

Accuracy of Diagnosis

Level III. Taking into account the patient's clinical status and tumor location, surgical resection should be carried out to maximize the chance of accurate diagnosis.

Question

What tools can improve the safety of surgery for low grade gliomas in eloquent locations?

Target Population

These recommendations apply to adults with imaging suggestive of a WHO grade II glioma (oligodendroglioma, astrocytoma, or oligo-astrocytoma).

Recommendations

Preoperative Imaging

Level III. It is recommended that preoperative functional MRI and diffusion tensor imaging be utilized in the appropriate clinical setting to improve functional outcome after surgery for low grade glioma.

Intraoperative Mapping of Tumors in Eloquent Areas

Level III. Intraoperative mapping is recommended for patients with diffuse low grade gliomas in eloquent locations compared to patients with non-eloquently located diffuse low grade gliomas as a way of preserving function.

Definitions

American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Classification of Evidence on Therapeutic Effectiveness and Levels of Recommendation

Evidence Classification	
Class I	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II	Evidence provided by well-designed observational studies with concurrent controls (e.g., case control and cohort studies)
Class III	Evidence provided by expert opinion, case series, case reports and studies with historical controls
Levels of Recommendation	
Level 1	Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires Class I evidence which directly addresses the clinical questions or overwhelming Class II evidence when circumstances preclude randomized clinical trials)
Level 2	Recommendations for patient management which reflect clinical certainty (usually this requires Class II evidence or a strong consensus of class III evidence)
Level 3	Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Diffuse low grade glioma (World Health Organization [WHO] grade II glioma [oligodendroglioma, astrocytoma, or oligo-astrocytoma])

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Neurological Surgery

Neurology

Oncology

Radiology

Intended Users

Physicians

Guideline Objective(s)

To systematically review the evidence available for surgical resection in the management of newly diagnosed low grade glioma

Target Population

Adults with imaging suggestive of a World Health Organization (WHO) grade II glioma (oligodendroglioma, astrocytoma, or oligo-astrocytoma)

Interventions and Practices Considered

1. Observation
2. Surgical resection (gross total resection or subtotal resection)
3. Biopsy alone
4. Intraoperative magnetic resonance imaging (MRI) during surgery
5. Preoperative functional MRI and diffusion tensor imaging
6. Intraoperative mapping of tumors in eloquent areas

Major Outcomes Considered

- Overall survival
- Progression free survival
- Recurrence rate
- Seizure control
- Tumor progression within 5 years of surgery
- Morbidity
- Mortality
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

General Search Strategy

Literature Examination Approach

A wide-ranging literature search strategy was undertaken to identify all citations relevant to the management of low grade gliomas. The MEDLINE and EMBASE electronic databases were searched from 1990 through 2012, with additional data being gleaned from the Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Registry, and Cochrane Database of Abstracts of Reviews of Effects. The search strategies used a combination of subheadings and text words with the specifics of this work being outlined in each guideline section. Reference lists of the publications chosen for full text review were also screened for potentially relevant studies.

Study Selection

The search of the bibliographic databases identified possibly relevant citations for a given topic and often these were large in number. The eligibility (inclusion/exclusion) criteria to screen the citations for each of the questions were determined ahead of time for each section by the writing group. At least two authors evaluated the titles and abstracts using the inclusion and exclusion criteria with broad interpretation of the criteria being used initially so as to maximize the likelihood of capturing pertinent information. Cases of disagreement about pertinence were resolved by a third author when needed. The full text articles of the selected abstracts were then collected and the same process of applying the eligibility criteria was carried out again with the more in depth information available. Articles that met the eligibility criteria were grouped according to the questions they addressed and used to create the evidence tables and scientific foundation sections. Reasons for exclusion for papers were also documented so as to be able to discuss pertinent problem citations in the scientific foundation as needed.

Specific Search Strategy for This Guideline

The following electronic databases were searched from 1990 to December 2012: PubMed, EMBASE, Cochrane Database of Systematic Reviews, and abstracts from the annual meetings of the Society for Neuro-Oncology (SNO), American Association of Neurologic Surgeons (AANS), and Congress of Neurologic Surgeons (CNS).

For PubMed the following search strings were input: low grade glioma surgery, low grade glioma craniotomy, and low grade glioma observation. For the Cochrane Library, the following search strings were used: Surgery/ and Brain Neoplasms/, Low Grade Glioma/, and Low Grade Glioma/ and Surgery/.

Eligibility Criteria

In order to be included, studies needed to be:

1. Published in English
2. Involve patients with newly diagnosed World Health Organization (WHO) grade II oligodendroglioma, astrocytoma, or oligo-astrocytoma or imaging suggestive of those diagnoses. In publications with mixed populations, the results of those with newly diagnosed WHO grade II tumor must be separable from others.
3. Fully-published peer-reviewed studies or meeting abstracts from national neurosurgical meetings (AANS or CNS) or the SNO annual meeting
4. Number of study participants with newly diagnosed WHO grade II tumor, or imaging suggestive of such a lesion, being five or higher
5. Enrolled adult patients (18 years of age and older) or provide isolated results for adult patients in a mixed cohort that can be assessed separately

Review or update articles were only read to make sure that pertinent studies they cited were captured during the PubMed search. The following exclusion criteria were applied to search results to obtain relevant articles for low grade glioma surgery: non-English publications, case series of less than 5 patients, new device articles, basic science papers, animal studies, high-grade glioma manuscripts, recurrent tumor articles, papers focusing exclusively on chemotherapy, papers focusing exclusively on radiation, anesthesia articles, pathologic analysis papers (e.g., immunohistochemical staining), papers studying pilocytic astrocytoma or ependymoma, and spinal cord tumors.

Study Selection

Two independent reviewers evaluated citations using a priori criteria for relevance and documented decisions in standardized forms. Cases of disagreement were resolved by a third reviewer. The same methodology was used for full-text screening of potentially relevant papers.

Number of Source Documents

Overall, 67 primary studies met the eligibility criteria for this systematic review, including 64 studies that produced class III data and 3 studies producing class II data related to surgery for low grade gliomas. Figure 1 in the original guideline document outlines the flow of studies through the review process.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Classification of Evidence on Therapeutic Effectiveness

Evidence Classification	
Class I	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II	Evidence provided by well-designed observational studies with concurrent controls (e.g., case control and cohort studies)
Class III	Evidence provided by expert opinion, case series, case reports and studies with historical controls

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

General Evidence Analysis

Quality Assessment and Statistical Methods

Articles that met the eligibility criteria were grouped according to the questions they addressed and used to create the evidence tables and scientific foundation sections. Reasons for exclusion for papers were also documented so as to be able to discuss pertinent problem citations in the scientific foundation as needed.

Studies which met the eligibility criteria were subject to more detailed scrutiny and had their data extracted by one reviewer and the extracted information was checked by one or more other reviewers. Evidence and summary tables, reporting the extracted study information and evidence classification, were generated for all of the included studies for each of the questions. Evidence tables were created with most recent data first and subsequent listings in retrograde chronological order. The table headings consisted of first author name and year, followed by a brief study description, chosen data class and conclusion. The authors were directed to craft the data in the tables in a succinct and fact filled manner so as to allow for understanding of the literature entry. The literature in the evidence tables was expanded upon in the scientific foundation of each section so as to emphasize important points supporting its classification and contribution to recommendations. The method by which this was accomplished is expanded upon in the Joint Guideline Committee Guideline Development Methodology document (see the "Availability of Companion Documents" field). Internal drafts of the tables and manuscripts were developed by sharing between writers electronically, by telephone and meetings. Summary and conclusion statements were included for each section, with comments on key issues for future investigation being added where pertinent.

Specific Evidence Analysis for This Guideline

Quality Assessment

Studies which met the eligibility criteria were data extracted by one reviewer and the extracted information was then checked by a second reviewer.

Evidence Classification and Recommendation Levels

Both the quality of the evidence and the strength of the recommendations were graded according to the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) criteria as noted in the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Guideline Panel Development

Recognizing the serious nature of low grade gliomas along with the lack of consensus among various treatment options, the Joint Tumor Section of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) recommended that evidence-based guidelines be developed as a top priority, for the diagnosis, management and treatment of low grade glioma patients. The objectives of these guidelines are to establish the best evidence-based management of low grade gliomas in terms of imaging diagnosis, use of surgical biopsy and resection, assessment of tumor pathology, administration of systemic chemotherapy, and administration of radiation therapy. Because these tumors dependably recur or progress despite standard therapy, the Joint Tumor Section also recommended an evidence-based guideline be developed for progressive low grade gliomas and that information on promising emerging therapies be assessed in the same manner to determine the possible application of these findings.

Having identified the topical objectives, the Guidelines Committee of the Joint Tumor Section then recruited experts in the field from each of the parent organizations as lead writers of each section. These writers, in turn, recruited experts in non-neurosurgical specialties relevant to the field of management and therapy chosen. Writers were provided training on the method of guideline development as used in this guideline set by written methods and instructions. The senior authors and CNS Guidelines Manager then worked with them on a step by step basis to confirm that the methods were followed as the literature was collected, assessed and documents developed. When writers were approached and preliminarily agreed to participate they were asked to complete a formal conflict of interest questionnaire confirming the appropriateness of their participation. At that point they also agreed to report any new conflicts of interest that might develop during the writing process. In this manner a multidisciplinary panel of writers referred to as the Low Grade Glioma Guidelines Task Force was assembled, with significant administrative, logistical and analytical support from the national CNS Guidelines Committee. The method of this evidence-based clinical practice parameter guideline has been written in a manner to be as transparent as possible using published assessment criteria.

Topic Range of This Systematic Review and Clinical Practice Guideline

Having identified writing groups for each topic, the members designed questions to allow assessment of the literature in a manner that would provide guidance for management of low grade gliomas. These questions are presented at the beginning of each of the eight guideline chapters spanning the topics of imaging assessment, diagnostic biopsy, surgical resection, tumor evaluation by standard neuropathology and molecular techniques, radiation therapy, chemotherapy, emerging therapies and treatment of recurrent or progressive low grade gliomas.

Guideline Panel Consensus

Multidisciplinary writing groups were created for each section based on author expertise, in order to address each of the disciplines and particular areas of therapy selected for these clinical guidelines. Each group was involved with literature selection, creation and editing of the evidence tables and scientific foundations for their specific section and discipline. Using this information, the writing groups then drafted the recommendations in answer to the questions formulated at the beginning of the process, culminating in the clinical practice guideline for their respective discipline. The draft guidelines were then circulated to the entire clinical guideline panel to allow for multidisciplinary feedback, discussion, and ultimately approval.

Rating Scheme for the Strength of the Recommendations

American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Classification of Levels of Recommendation

Levels of Recommendation	
Level 1	Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires Class I evidence which directly addresses the clinical questions or overwhelming Class II evidence when circumstances preclude randomized clinical trials)
Level 2	Recommendations for patient management which reflect clinical certainty (usually this requires Class II evidence or a strong consensus of class III evidence)
Level 3	Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Approval Process

The completed evidence-based clinical practice guidelines for the management of low grade gliomas were presented to the Joint Guidelines Committee of the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) for review. The reviewers for the Joint Guidelines Committee were vetted by the *Journal of Neuro-oncology* for suitability and expertise to serve as reviewers for the purposes of publication in that journal also. The final product was then approved and endorsed by the executive committees of both the AANS and CNS prior to publication in the *Journal of Neuro-oncology*.

The funding agencies (CNS Executive Committee and AANS/CNS Joint Tumor Section Executive Committee) were permitted to review these guidelines only after the Joint Guidelines Committee had completed its extensive review, critique and ultimate approval process; the funding groups then were limited to whether or not to endorse or reject this body of work but substantive changes were not allowed.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

While the lack of class I evidence and limited examples of class II evidence restricts the Task Force's ability to definitively recommend surgery for low grade gliomas, the literature is supportive of several potential benefits of surgery for patients with diffuse low grade gliomas. The three examples of class II evidence support the lack of a negative impact from a wait and see approach on cognitive performance and quality of life, less frequent tumor progression with gross total resection (GTR) or subtotal resection (STR) compared to biopsy alone, and a surprisingly high rate of progression even after GTR. Most of the class III evidence supports a benefit of surgery on survival, with the impact of surgery being greater on progression-free survival (PFS) (with 17 of 19 [89%] studies supporting some benefit of surgery on PFS) than on overall survival (OS) (for with 26 of 34 [76%] studies supporting a benefit of surgery). Class III studies also promote benefits of surgery on seizure control and accuracy of pathology, and suggest that plasticity and neuro-monitoring can improve functional outcomes after surgery for low grade gliomas in eloquent locations.

For additional potential benefits, please refer to Table 1 in the original guideline document.

Potential Harms

- In one retrospective cohort study reviewing a consecutive series of patients whose imaging studies suggested glioma and who underwent stereotactic biopsy at outside hospitals followed by craniotomy/resection at the authors' tertiary center (within 60 days), major neurologic complications occurred in 10 (12.3%) of 81 surgical patients and 3 (3.7%) of 81 patients undergoing biopsy.

- The authors of a retrospective summary of experience with microsurgical resection of insular tumors concluded that insular tumor surgery carries substantial complication rates.
- Risk of either recurrence or death for neurosurgical patients who undergo resection of low grade glioma using intraoperative magnetic resonance imaging (iMRI) guidance

For additional potential harms, please refer to Table 1 in the original guideline document.

Qualifying Statements

Qualifying Statements

The information in these guidelines reflects the current state of knowledge at the time of completion. Each section is designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Aghi MK, Nahed BV, Sloan AE, Ryken TC, Kalkanis SN, Olson JJ. The role of surgery in the management of patients with diffuse low grade glioma: a systematic review and evidence-based clinical practice guideline. J Neurooncol. 2015 Dec;125(3):503-30. [69 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Dec

Guideline Developer(s)

American Association of Neurological Surgeons - Medical Specialty Society

Congress of Neurological Surgeons - Professional Association

Source(s) of Funding

These guidelines were funded exclusively by the Congress of Neurological Surgeons (CNS) Guidelines Committee, with no funding from any outside commercial sources. Development of this set of evidence-based clinical practice guidelines was editorially independent from the funding agencies.

Guideline Committee

American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Joint Guidelines Committee

Low Grade Glioma Guidelines Task Force

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Conflict of Interest

Low Grade Glioma Guidelines Task Force members were required to report all possible conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Joint Guidelines Committee, including potential COIs that are unrelated to the topic of the guideline. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of Task Force Members with possible conflicts and address this by restricting the writing and reviewing privileges of that person to topics unrelated to the possible COIs.

Disclosures

Dr. Kalkanis is a consultant for Arbor and Varian. Dr. Olson is a consultant for the American Cancer Society; has received research funding from the National Cancer Institute, Genentech, and Millennium; and has received investigational drug provision from Merck.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Neuro-Oncology Web site.

Availability of Companion Documents

The following are available:

- Rock J. Low grade glioma guidelines: foreword. J Neurooncol. 2015 Dec;125(3):447-8. Available from the Journal of Neuro-Oncology Web site.
- Olson JJ, Kalkanis SN, Ryken TC. Evidence-based clinical practice parameter guidelines for the treatment of adults with diffuse low grade glioma: introduction and methods. J Neurooncol. 2015 Dec;125(3):449-56. Available from the Journal of Neuro-Oncology Web site.
- Congress of Neurological Surgeons (CNS). Guideline development methodology: endorsed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the AANS/CNS Joint Guideline Committee. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2012 Feb. 12 p. [2 references]. Available from the Congress of Neurological Surgeons Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 7, 2016. The information was not verified by the guideline developer.

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